[APSAVD] APSAVD Young Investigators Award Session

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Hiroaki Okazaki（Department of Diabetes and Metabolic Diseases, The University of Tokyo, Japan）
Lourdes Ella Santos（Cardinal Santos Medical Center, Philippines）

英語

英語セッション

YIA-5

Comprehensive Genetic Analysis in Patients with Familial Hyperchylomicronemia Using a Next Generation Sequencing Panel

Hayato Tada:1、Ryota Teramoto:1、Masa-aki Kawashiri:1、Atsushi Nohara:2、Akihiro Inazu:3、Hiroshi Mabuchi:2、Masakazu Yamagishi:1
1:Division of Cardiovascular Medicine, Kanazawa University, Kanazawa, Japan、2:Department of Advanced Research in Community Medicine, Kanazawa University Graduate School of Medical Sciences、3:Department of Laboratory Science, Molecular Biochemistry and Molecular Biology, Graduate School of Medical Science, Kanazawa University

Background: Familial hyperchylomicronemia is a rare autosomal recessive disorder exhibiting severe hypertriglyceridemia due to mutations in the lipoprotein lipase (LPL)-associated genes. Few data exist regarding the comprehensive genetic approach using next-generation sequencing to uncover the causative genetic mutations.
Methods: We performed a targeted next-generation sequencing on panel comprising 4, 813 genes associated with known clinical phenotypes. Eight patients with clinical diagnosis of familial hyperchylomicronemia were analyzed (male = 2, mean age = 36.9 years, mean triglyceride level = 1, 319.3 mg/dl). We filtered out such variants as 1) benign variants, 2) minor allele frequency >1% and 3) Combined Annotation Dependent Depletion score <10.
Results: A total of 73, 389 variants were found with 94.3% of mean coverage (> ×20), of which 1, 289 were missense, frameshift, in-frame deletion and splice-site. Our schema could reduce the number of candidate to 4 causative homozygous mutations in LPL gene (p.Ala248Leu, p.Arg270Cys, p.Ala361Thr and p.Val227Gly) including 2 novel mutations in 4 out of 8 individuals (50%). Patients with homozygous mutation in LPL gene showed significantly higher level of triglyceride compared with those without mutation in LPL gene (2, 444.8 mg/dl vs 193.8 mg/dl, p=0.029).
Conclusion: We could successfully determine causative mutations in 4 out of 8 individuals (50%) exhibiting familial hyperchylomicronemia. Targeted next-generation sequencing panel is an efficient tool for genetic diagnosis of familial hyperchylomicronemia, which could provide appropriate therapies.